General

Guideline Title

Locally advanced, unresectable pancreatic cancer: American Society of Clinical Oncology clinical practice guideline.

Bibliographic Source(s)

Balaban EP, Mangu PB, Khorana AA, Shah MA, Mukherjee S, Crane CH, Javle MM, Eads JR, Allen P, Ko AH, Engebretson A, Herman JM, Strickler JH, Benson AB III, Urba S, Yee NS. Locally advanced, unresectable pancreatic cancer: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2016 Aug 1;34(22):2654-68. [75 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- August 31, 2016 – Opioid pain and cough medicines combined with benzodiazepines : A U.S. Food and Drug Administration (FDA) review has found that the growing combined used of opioid medicines with benzodiazepines or other drugs that depress the central nervous system (CNS) has resulted in serious side effects, including slowed or difficult breathing and deaths. FDA is adding Boxed Warnings to the drug labeling of prescription opioid pain and prescription opioid cough medicines and benzodiazepines.
- March 22, 2016 – Opioid pain medicines : The U.S. Food and Drug Administration (FDA) is warning about several safety issues with the entire class of opioid pain medicines. These safety risks are potentially harmful interactions with numerous other medications, problems with the adrenal glands, and decreased sex hormone levels. They are requiring changes to the labels of all opioid drugs to warn about these risks.

Recommendations

Major Recommendations

Definitions for the rating of evidence (High, Intermediate, Low, Insufficient); types of recommendations (Evidence based, Formal consensus,

Informal consensus, No recommendation); and strength of recommendations (Strong, Moderate, Weak) are provided at the end of the "Major Recommendations" field.

Clinical Question 1

After a histopathologic confirmation of pancreatic adenocarcinoma diagnosis, what initial assessment is recommended before initiating therapy for locally advanced, unresectable pancreatic cancer (LAPC)?

Recommendation 1.1

A multiphase computed tomography (CT) scan of the chest, abdomen, and pelvis should be performed to assess extent of disease. Other staging studies should be performed only as dictated by symptoms (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Recommendation 1.2

The baseline performance status (PS), symptom burden, and comorbidity profile of a patient diagnosed with LAPC should be carefully evaluated (Type: evidence based, benefits outweigh harms; Evidence quality: high; Strength of recommendation: strong).

Recommendation 1.3

The goals of care (including a discussion of an advance directive), patient preferences, as well as support systems should be discussed with every person diagnosed with LAPC and his or her caregivers (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Recommendation 1.4

Multidisciplinary collaboration to formulate treatment and care plans and disease management for patients with LAPC should be the standard of care (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Recommendation 1.5

Every person with pancreatic cancer should be offered information about clinical trials—therapeutic trials in all lines of treatment, as well as palliative care, biorepository/biomarker, and observational studies (Type: informal consensus, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Clinical Question 2

What is the appropriate initial treatment approach for people diagnosed with LAPC?

Recommendation 2.1

Initial systemic therapy with combination regimens is recommended for most patients who meet the following criteria: Eastern Cooperative Oncology Group (ECOG) PS 0 or 1, a favorable comorbidity profile, and patient preference and a support system for aggressive medical therapy. There is no clear evidence to support one regimen over another, and physicians may offer therapy on the basis of extrapolation from data derived from studies in the metastatic setting. For some patients, conformal radiation therapy (CRT) or stereotactic body radiotherapy (SBRT) may be offered up front, on the basis of patient and physician preference (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Clinical Question 3

Which patients with LAPC may be offered radiation therapy (CRT/SBRT)?

Recommendation 3.1

If there is local disease progression after induction chemotherapy, but without evidence of systemic spread, then CRT may be offered to patients who meet the following criteria: first-line chemotherapy treatment is completed or terminated; ECOG PS ≤ 2; a comorbidity profile that is adequate, including adequate hepatic and renal function and hematologic status; and patient preference (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Recommendation 3.2

CRT may be offered to patients who have responded to an initial 6 months of chemotherapy or have stable disease, or have developed unacceptable chemotherapy-related toxicities or show a decline in PS as a consequence of chemotherapy toxicity (Type: evidence-based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Recommendation 3.3

If there is response or stable disease after 6 months of induction chemotherapy, CRT may be offered as an alternative to continuing chemotherapy alone for any patient with LAPC (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Clinical Question 4

Which people with LAPC may be initially offered SBRT?

Recommendation 4.1

Clinicians may offer SBRT for treatment of patients with LAPC, although the evidence quality is intermediate so additional prospective and/or randomized trials are required to definitively compare results of SBRT with chemotherapy alone and SBRT (Type: informal consensus, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate).

Clinical Question 5

Which people with LAPC whose disease has progressed (abdominal pain, worsening jaundice, increase in size of tumor and/or new metastatic lesions on imaging study; persistently increasing serum cancer antigen [CA] 19-9) should be offered additional treatment per the ASCO metastatic pancreatic cancer guideline?

Recommendation 5.1

All people who have not benefited from first-line treatment and have disease progression should be offered treatment per the American Society of Clinical Oncology (ASCO) Metastatic Pancreatic Cancer Treatment Guideline. See the National Guideline Clearinghouse (NGC) summary of the ASCO guideline Metastatic pancreatic cancer and the summary table of recommendations for metastatic pancreatic cancer in the Data Supplement (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate).

Recommendation 5.2

Refer people with LAPC who have not benefited from treatment and have disease progression for a clinical trial (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Clinical Question 6

When should the concept of palliative care be introduced? When should a palliative care consult be initiated?

Recommendation 6.1

People with LAPC should have a full assessment of symptom burden, psychological status, and social supports, as early as possible—preferably at the first visit. In most cases, this will indicate a need for a formal palliative care consult and services (Type: evidence based, benefits outweigh harms; Evidence quality: moderate; Strength of recommendation: strong).

Clinical Question 7

For people with LAPC, what are the recommended strategies for relief of pain and symptom burden?

Recommendation 7.1

People with LAPC should be offered aggressive treatment of the pain and other symptoms of the cancer and/or cancer-directed therapy (Type: evidence based, benefits outweigh harms; Evidence quality: moderate; Strength of recommendation: strong).

Recommendation 7.2

A short course of palliative radiotherapy (conventional RT or SBRT) may be offered to patients with LAPC who meet the following criteria: prominent local symptoms, such as abdominal pain and/or worsening jaundice and/or gastrointestinal (GI) bleeding; local infiltration into the GI tract causing impending gastric outlet or duodenal obstruction; and patient preference (Type: evidence based, benefits outweigh harms; Evidence

quality: intermediate; Strength of recommendation: moderate).

Clinical Question 8

What is the recommended frequency of follow-up care/surveillance for people with LAPC?

Recommendation 8.1

In the absence of RCT evidence, the Panel consensus is that patients with LAPC who have completed treatment and have stable disease or no disease progression schedule follow-up visits every 2 to 3 months that include a physical examination and liver and renal function laboratory testing for a 2-year duration. The intervals can then be increased to every 6 months (Type: Informal consensus, benefits outweigh harms; Evidence quality: low; Strength of recommendation: strong).

Recommendation 8.2

Data are not definitive, but the Panel recommends testing markers (CA 19-9) and imaging (CT) should be performed at least every 3 months during the first 2 years. Imaging intervals can be increased to every 6 months once stability is comfortably established. The routine use of positron emission tomography/CT imaging for the management of LAPC is not recommended. Tumor markers such as CA 19-9 should not replace imaging as an assessment (Type: Informal consensus, benefits outweigh harms; Evidence quality: low; Strength of recommendation: strong).

Definitions

Guide for Rating Quality of Evidence

Rating for Strength of Evidence	Definition
High	High confidence that the available evidence reflects the true magnitude and direction of the net effect (i.e., balance of benefits versus harms) and that further research is very unlikely to change either the magnitude or direction of this net effect.
Intermediate	Moderate confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research is unlikely to alter the direction of the net effect; however, it might alter the magnitude of the net effect.
Low	Low confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research may change either the magnitude and/or direction of this net effect.
Insufficient	Evidence is insufficient to discern the true magnitude and direction of the net effect. Further research may better inform the topic. The use of the consensus opinion of experts is reasonable to inform outcomes related to the topic.

Guide for Types of Recommendations

Type of Recommendation	Definition
Evidence based	There was sufficient evidence from published studies to inform a recommendation to guide clinical practice.
Formal consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. Therefore, the Expert Panel used a formal consensus process to reach this recommendation, which is considered the best current guidance for practice. The Panel may choose to provide a rating for the strength of the recommendation (i.e., "strong," "moderate," or "weak"). The results of the formal consensus process are summarized in the guideline and reported in the Data Supplement (see the "Availability of Companion Documents" field).
Informal consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. The recommendation is considered the best current guidance for practice, based on informal consensus of the Expert Panel. The Panel agreed that a formal consensus process was not necessary for reasons described in the literature review and discussion. The Panel may choose to provide a rating for the strength of the recommendation (i.e., "strong," "moderate," or "weak").
No recommendation	There is insufficient evidence, confidence, or agreement to provide a recommendation to guide clinical practice at this time. The Panel deemed the available evidence as insufficient and concluded it was unlikely that a formal consensus process would achieve the level of agreement needed for a recommendation.

Guide for Strength of Recommendations

Rating for Strength of Recommendation	Definition
Strong	There is high confidence that the recommendation reflects best practice. This is based on (1) strong evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with no or minor exceptions; (3) minor or no concerns about study quality; and/or (4) the extent of panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a strong recommendation.
Moderate	There is moderate confidence that the recommendation reflects best practice. This is based on (1) good evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with minor and/or few exceptions; (3) minor and/or few concerns about study quality; and/or (4) the extent of panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a moderate recommendation.
Weak	There is some confidence that the recommendation offers the best current guidance for practice. This is based on (1) limited evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, but with important exceptions; (3) concerns about study quality; and/or (4) the extent of panelists' agreement. Other considerations (discussed in the guideline's literature review and analyses) may also warrant a weak recommendation.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Locally advanced, unresectable pancreatic cancer

Guideline Category

Evaluation

Management

Treatment

Clinical Specialty

Gastroenterology

Oncology

Radiation Oncology

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To provide evidence-based recommendations to oncologists and others for treatment of patients with locally advanced, unresectable pancreatic cancer (LAPC)
- To help with clinical decision making, including determining the appropriate treatment of people with LAPC and how to help patients and their families to access and use palliative care services

Target Population

Patients diagnosed with locally advanced, unresectable pancreatic cancer (LAPC)

Interventions and Practices Considered

Evaluation

1. Multiphase computed tomography (CT) scan of the chest, abdomen, and pelvis
2. Evaluation of baseline performance status, symptom burden, and comorbidity profile
3. Discussion of goals of care (including a discussion of an advance directive), patient preferences, and support systems
4. Early full assessment of symptom burden, psychological status, and social supports

Treatment/Management

1. Multidisciplinary collaboration to formulate treatment and care plans and disease management
2. Offering patients information about clinical trials - therapeutic trials in all lines of treatment, as well as palliative care, biorepository/biomarker, and observational studies
3. Initial systemic therapy with combination regimens
4. Conformal radiation therapy (CRT) or stereotactic body radiotherapy (SBRT)
5. Chemoradiotherapy for certain patient groups
6. Treatment for metastatic disease according to established guidelines
7. Referring patients to clinical trials
8. Aggressive treatment for pain and other symptoms
9. Palliative radiotherapy (conventional RT or SBRT)
10. Frequency of follow-up physical exam and liver and renal function laboratory testing
11. Frequency of follow-up testing of markers (cancer antigen [CA] 19-9) and imaging (CT) (positron emission tomography [PET]/CT] not recommended)

Major Outcomes Considered

- Response rate
- Overall survival
- Disease-free survival
- Progression-free survival
- Adverse events

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Guideline Development Process

The recommendations were developed by the multidisciplinary Expert Panel using a systematic review of articles (April 2002 to June 2015) of phase III randomized controlled trials (RCTs). Other peer-reviewed articles were used to inform the recommendations on palliative care and patient and clinical communication as well as the section on health disparities. Articles were selected for inclusion in the systematic review of the evidence on the basis of the following criteria: patients with locally advanced, unresectable pancreatic cancer (LAPC), phase III RCTs of chemotherapy alone and/or with chemoradiotherapy and/or compared with a control arm, in English, and with human subjects.

Articles were excluded from the systematic review if they were meeting abstracts not subsequently published in peer-reviewed journals; editorials, commentaries, letters, news articles, case reports, or narrative reviews; or published in a non-English language.

Literature Search Strategy

Computerized literature searches of MEDLINE and the Cochrane Collaboration Library were performed. The searches of the English-language literature published from January 2000 to June 2015 combined pancreatic neoplasm terms and follow-up-related terms and MeSH headings. Results of the databases searches were supplemented with hand searching of the bibliographies of systematic reviews and selected seminal articles, and contributions from Expert Panel members' personal files.

Details of the literature search strategy are provided in Data Supplement 3 (see the "Availability of Companion Documents" field). A Quality of Reporting of Meta-analyses (QUOROM) Diagram illustrating the article selection process is available in Data Supplement 4 (see the "Availability of Companion Documents" field).

Number of Source Documents

There were 26 randomized controlled trials (RCTs) that met eligibility criteria and form the evidentiary basis for some of the guideline recommendations. Fourteen systematic reviews or meta-analyses of various rigor and quality were obtained; none were deemed suitable as the basis for recommendations.

See the Quality of Reporting of Meta-analyses (QUOROM) Diagram (Data Supplement 4) in the Data Supplement (see the "Availability of Companion Documents" field) for an outline of the study selection process.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Guide for Rating Quality of Evidence

Rating for Strength of Evidence	Definition
High	High confidence that the available evidence reflects the true magnitude and direction of the net effect (i.e., balance of benefits versus harms) and that further research is very unlikely to change either the magnitude or direction of this net effect.
Intermediate	Moderate confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research is unlikely to alter the direction of the net effect; however, it might alter the magnitude of the net effect.
Low	Low confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research may change either the magnitude and/or direction of this net effect.
Insufficient	Evidence is insufficient to discern the true magnitude and direction of the net effect. Further research may better inform the topic. The use of the consensus opinion of experts is reasonable to inform outcomes related to the topic.

Guide for Rating of Potential for Bias

Rating of Potential for Bias	Definitions for Rating Potential for Risk of Bias in Randomized Controlled Trials
Low risk	No major features in the study that risk biased results, and none of the limitations are thought to decrease the validity of the conclusions. The study avoids problems such as failure to apply true randomization, selection of a population unrepresentative of the target patients, high dropout rates, and no intention-to-treat analysis; and key study features are described clearly (including the population, setting, interventions, comparison groups, measurement of outcomes, and reasons for dropouts).
Intermediate	The study is susceptible to some bias, but flaws are not sufficient to invalidate the results. Enough of the items introduce some uncertainty about the validity of the conclusions. The study does not meet all the criteria required for a rating of good quality, but no flaw is likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.
High risk	There are significant flaws that imply biases of various types that may invalidate the results. Several of the items introduce serious uncertainty about the validity of the conclusions. The study has serious errors in design, analysis, or reporting; large amounts of missing information; or discrepancies in reporting.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Data Extraction

Literature search results were reviewed and deemed appropriate for full text review by two American Society of Clinical Oncology (ASCO) staff reviewers in consultation with the Expert Panel Co-Chairs. Data were extracted by two staff reviewers and subsequently checked for accuracy through an audit of the data by another ASCO staff member. Disagreements were resolved through discussion and consultation with the Co-Chairs if necessary. Evidence tables are provided in Data Supplements 1 and 2 (see the "Availability of Companion Documents" field).

Study Quality Assessment

Study design aspects related to individual study quality, strength of evidence, strength of recommendations, and risk of bias were assessed and are shown in Data Supplement 1, Table 2. The study quality was high for this group of randomized controlled trials (RCTs). Design aspects related to the individual study quality were assessed with factors such as blinding, allocation concealment, placebo control, intention to treat, funding sources, and so on generally indicating a low potential risk of bias for most of the identified evidence. Follow-up times varied between studies, decreasing the comparability of the results. Refer to the "Rating Scheme for the Strength of the Evidence" and "Rating Scheme for the Strength of the Recommendations" fields for definitions of ratings of evidence quality, strength of recommendations, and overall potential risk of bias.

Methods Used to Formulate the Recommendations

Expert Consensus

Informal Consensus

Description of Methods Used to Formulate the Recommendations

Panel Composition

The American Society of Clinical Oncology (ASCO) Clinical Practice Guidelines Committee (CPGC) convened an Expert Panel with multidisciplinary representation in medical oncology, radiation oncology, surgical oncology, pathology, community oncology, patient/advocacy representation, and guideline implementation. The Expert Panel was led by two Co-Chairs who had primary responsibility for the development and

timely completion of the guideline.

Guideline Development Process

The Expert Panel met via webinar on several occasions and corresponded frequently through e-mail; progress on guideline development was driven primarily by the Co-Chairs along with ASCO staff. The purpose of the meetings was for members to contribute content, provide critical review, interpret evidence, and finalize the guideline recommendations based upon the consideration of the evidence. All members of the Expert Panel participated in the preparation of the draft guideline document.

Development of Recommendations

The guideline recommendations were crafted, in part, using the GuideLines Into DEcision Support (GLIDES) methodology and accompanying BRIDGE-Wiz software™. This method helps guideline panels systematically develop clear, translatable, and implementable recommendations using natural language, based on the evidence and assessment of its quality to increase usability for end users. The process incorporates distilling the actions involved, identifying who will carry them out, to whom, under what circumstances, and clarifying if and how end users can carry out the actions consistently. This process helps the Panel focus the discussion, avoid using unnecessary and/or ambiguous language, and clearly state its intentions.

Some recommendations are based on informal consensus by the Panel, because there was no RCT evidence.

Rating Scheme for the Strength of the Recommendations

Guide for Types of Recommendations

Type of Recommendation	Definition
Evidence based	There was sufficient evidence from published studies to inform a recommendation to guide clinical practice.
Formal consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. Therefore, the Expert Panel used a formal consensus process to reach this recommendation, which is considered the best current guidance for practice. The Panel may choose to provide a rating for the strength of the recommendation (i.e., "strong," "moderate," or "weak"). The results of the formal consensus process are summarized in the guideline and reported in the Data Supplement (see the "Availability of Companion Documents" field).
Informal consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. The recommendation is considered the best current guidance for practice, based on informal consensus of the Expert Panel. The Panel agreed that a formal consensus process was not necessary for reasons described in the literature review and discussion. The Panel may choose to provide a rating for the strength of the recommendation (i.e., "strong," "moderate," or "weak").
No recommendation	There is insufficient evidence, confidence, or agreement to provide a recommendation to guide clinical practice at this time. The Panel deemed the available evidence as insufficient and concluded it was unlikely that a formal consensus process would achieve the level of agreement needed for a recommendation.

Guide for Strength of Recommendations

Rating for Strength of Recommendation	Definition
Strong	There is high confidence that the recommendation reflects best practice. This is based on (1) strong evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with no or minor exceptions; (3) minor or no concerns about study quality; and/or (4) the extent of panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a strong recommendation.
Moderate	There is moderate confidence that the recommendation reflects best practice. This is based on (1) good evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with minor and/or few exceptions; (3) minor and/or few concerns about study quality; and/or (4) the extent of panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a moderate recommendation.
Weak	There is some confidence that the recommendation offers the best current guidance for practice. This is based on (1) limited evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, but with important exceptions;

Rating for Strength of Recommendation	Definition
	(3) concerns about study quality; and/or (4) the extent of panelists' agreement. Other considerations (discussed in the guideline's literature review and analyses) may also warrant a weak recommendation.

Cost Analysis

Cost Implications

There are limited cost-effectiveness analyses regarding the various treatment modalities used in the multidisciplinary management of locally advanced, unresectable pancreatic cancer (LAPC). However, the available data seem to support the recommendations outlined in the guideline.

One study (LAPC and metastatic pancreatic cancer) found in elderly patients that radiation plus fluorouracil had a cost-effectiveness ratio of $68,724/quality-adjusted life year (QALY) relative to no treatment and suggested that radiation plus gemcitabine would be cost effective as well. Another study (LAPC and metastatic pancreatic cancer) focused on the high cost of radiotherapy with the limited survival of pancreatic cancer. Compared with gemcitabine alone, gemcitabine plus stereotactic body radiation therapy (SBRT) had an incremental cost-effectiveness ratio (ICER) of $69,500/QALY, whereas gemcitabine plus conventional radiotherapy versus gemcitabine alone had an ICER of $126,800/QALY, and gemcitabine plus intensity modulated radiation therapy versus gemcitabine plus conventional radiotherapy had an ICER of $1,584,100/QALY. The authors concluded that these results indicated gemcitabine plus intensity-modulated radiation therapy (IMRT) exceeded society's cost-effectiveness standards, and gemcitabine plus SBRT provided a clinical benefit potentially acceptable by cost-effectiveness standards. Further studies are needed to understand the cost effectiveness of all treatment options for those patients diagnosed with LAPC.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Members of the Expert Panel are responsible for reviewing and approving the penultimate version of the guideline, which is then circulated for external review and submitted to *Journal of Clinical Oncology* for editorial review and consideration for publication. All American Society of Clinical Oncology (ASCO) guidelines are ultimately reviewed and approved by the Expert Panel and the ASCO Clinical Practice Guideline Committee before publication. The Clinical Practice Guideline Committee approved this guideline on January 25, 2016.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

The goals of treatment of patients with locally advanced, unresectable pancreatic cancer (LAPC) are controlling disease progression, symptoms, and the maintenance of quality of life (QOL). The oncologist should discuss the competing impact of disease progression and treatment toxicity on survival and QOL, including performance status (PS), and address the patient and caregiver's preferences of people being treated with LAPC. The guideline recommendations focus on improved clinical decision making, including determining the appropriate treatment of people with LAPC, and how to help patients and their families to access and use palliative care services.

Refer to the "Literature review and analysis" and "Clinical interpretation" sections of the original guideline document for a discussion of the potential

benefits and harms of each recommendation.

Potential Harms

Even in clinical trials, which enroll highly selected people, tolerance of and completion of therapy is challenging because of adverse events and toxicities.

The Data Supplement (see the "Availability of Companion Documents" field) provides details about randomized controlled trials and treatment regimens and overall survival, progression-free survival, adverse events, and quality of life for people with locally advanced, unresectable pancreatic cancer.

Refer to the "Literature review and analysis" and "Clinical interpretation" sections of the original guideline document for a discussion of the potential benefits and harms of each recommendation.

Contraindications

Contraindications

- The comorbidity profile can influence choice of chemotherapy agent; for example, avoid fluoropyrimidine-based regimens in patients with a known history of uncontrolled coronary artery disease.
- Stereotactic body radiation therapy (SBRT) should be avoided when tumors directly invade the bowel and/or stomach on endoscopic evaluation.

Qualifying Statements

Qualifying Statements

- The clinical practice guidelines and other guidance published herein are provided by the American Society of Clinical Oncology, Inc. (ASCO) to assist providers in clinical decision making. The information herein should not be relied upon as being complete or accurate, nor should it be considered as inclusive of all proper treatments or methods of care or as a statement of the standard of care. With the rapid development of scientific knowledge, new evidence may emerge between the time information is developed and when it is published or read. The information is not continually updated and may not reflect the most recent evidence. The information addresses only the topics specifically identified therein and is not applicable to other interventions, diseases, or stages of diseases. This information does not mandate any particular course of medical care. Further, the information is not intended to substitute for the independent professional judgment of the treating provider, as the information does not account for individual variation among patients. Recommendations reflect high, moderate, or low confidence that the recommendation reflects the net effect of a given course of action. The use of words like "must," "must not," "should," and "should not" indicates that a course of action is recommended or not recommended for either most or many cases, but there is latitude for the treating physician to select other courses of action in individual patients. In all cases, the selected course of action should be considered by the treating provider in the context of treating the individual patient. Use of the information is voluntary. ASCO provides this information on an "as is" basis and makes no warranty, express or implied, regarding the information. ASCO specifically disclaims any warranties of merchantability or fitness for a particular use or purpose. ASCO assumes no responsibility for any injury or damage to persons or property arising out of or related to any use of this information, or for any errors or omissions.
- Refer to the "Health Disparities," "MCCs" and "Limitation of the Research and Future Directions" sections in the original guideline document for additional qualifying information.

Implementation of the Guideline

Description of Implementation Strategy

Guideline Implementation

American Society of Clinical Oncology (ASCO) guidelines are developed for implementation across health settings. Barriers to implementation include the need to increase awareness of the guideline recommendations among front-line practitioners and survivors of cancer and caregivers and also to provide adequate services in the face of limited resources. The guideline Bottom Line was designed to facilitate implementation of recommendations. This guideline will be distributed widely through the ASCO Practice Guideline Implementation Network. ASCO guidelines are posted on the ASCO Web site and most often published in *Journal of Clinical Oncology* (*JCO*) and *Journal of Oncology Practice*.

For additional information on the ASCO implementation strategy, please see the ASCO Web site.

Implementation Tools

Patient Resources

Quick Reference Guides/Physician Guides

Slide Presentation

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

End of Life Care

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Balaban EP, Mangu PB, Khorana AA, Shah MA, Mukherjee S, Crane CH, Javle MM, Eads JR, Allen P, Ko AH, Engebretson A, Herman JM, Strickler JH, Benson AB III, Urba S, Yee NS. Locally advanced, unresectable pancreatic cancer: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2016 Aug 1;34(22):2654-68. [75 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Aug 1

Guideline Developer(s)

American Society of Clinical Oncology - Medical Specialty Society

Source(s) of Funding

American Society of Clinical Oncology (ASCO)

Guideline Committee

Locally Advanced, Unresectable Pancreatic Cancer Guideline Expert Panel

Composition of Group That Authored the Guideline

Expert Panel Members: Edward P. Balaban, DO (*Co-chair*), Private practice, State College, PA, Penn State Hershey Cancer Institute, Hershey, PA; Nelson S. Yee, MD (*Co-chair*), Penn State Hershey Cancer Institute, Hershey, PA; Alok A. Khorana, MD, Cleveland Clinic, Cleveland, OH; Manish A. Shah, MD, The Weill Cornell Medical Center, New York, NY; Somnath Mukherjee, MD, University of Oxford, Oxford, United Kingdom; Christopher H. Crane, MD, The University of Texas MD Anderson Cancer Center, Houston, TX; Milind M. Javle, MD, The University of Texas MD Anderson Cancer Center, Houston, TX; Jennifer R. Eads, MD, University Hospitals Seidman Cancer Center, Case Western Reserve University, Cleveland, OH; Peter Allen, MD, Memorial Sloan Kettering Cancer Center, New York, NY; Andrew H. Ko, MD University of California San Francisco Comprehensive Cancer Center, San Francisco, CA; Anitra Engebretson, patient representative, Portland, OR; Joseph M. Herman, MD, MS, Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD; John H. Strickler, MD, Duke University Medical Center, Durham, NC; Al B. Benson III, MD, Lurie Comprehensive Cancer Center of Northwestern, Chicago, IL; Susan Urba, MD, University of Michigan Cancer Center, Ann Arbor, MI; Pamela B. Mangu, MA, American Society of Clinical Oncology (ASCO) staff

Financial Disclosures/Conflicts of Interest

Guideline and Conflicts of Interest

The Expert Panel was assembled in accordance with the American Society of Clinical Oncology's (ASCO's) Conflict of Interest Policy Implementation for Clinical Practice Guidelines ("Policy," found at http://www.asco.org/rwc). All members of the Panel completed ASCO's disclosure form, which requires disclosure of financial and other interests, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as a result of promulgation of the guideline. Categories for disclosure include employment; leadership; stock or other ownership; honoraria; consulting or advisory role; speakers' bureau; research funding; patents, royalties, other intellectual property; expert testimony; travel, accommodations, expenses; and other relationships. In accordance with the Policy, the majority of the members of the Panel did not disclose any relationships constituting a conflict under the Policy.

Authors' Disclosures and Potential Conflicts of Interest

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or jco.ascopubs.org/site/ifc .

Edward P. Balaban
Consulting or Advisory Role: Truven Health Analytics

Pamela B. Mangu
No relationship to disclose

Alok A. Khorana
Honoraria: Sanofi, LEO Pharma, AngioDynamics, Genentech, Daiichi Sankyo, Janssen Pharmaceuticals, Boehringer Ingelheim, Halozyme Therapeutics, Pfizer
Consulting or Advisory Role: Sanofi, LEO Pharma, AngioDynamics, Daiichi Sankyo, Genentech, Janssen Pharmaceuticals, Boehringer Ingelheim, Halozyme Therapeutics
Research Funding: LEO Pharma, Amgen (Inst)
Travel, Accommodations, Expenses: Janssen Pharmaceuticals, AngioDynamics, Halozyme Therapeutics

Manish A. Shah
Consulting or Advisory Role: Eli Lilly
Research Funding: Eli Lilly/ImClone Systems (Inst), Gilead Sciences (Inst), Merck (Inst), BERG (Inst)

Somnath Mukherjee
Honoraria: Celgene
Consulting or Advisory Role: Celgene
Research Funding: Celgene
Travel, Accommodations, Expenses: Celgene

Christopher H. Crane
Honoraria: Vertex Pharmaceuticals, EMD Serono
Consulting or Advisory Role: Vertex Pharmaceuticals, EMD Serono

Milind M. Javle
No relationship to disclose

Jennifer R. Eads
Consulting or Advisory Role: Portola Pharmaceuticals, Saatchi Wellness, Oxigene
Research Funding: Novartis, AstraZeneca, HealthCare Pharmaceuticals (Inst), Bayer (Inst), Merck (Inst)
Travel, Accommodations, Expenses: Amgen Peter Allen
Consulting or Advisory Role: Sanofi
Research Funding: Novartis

Andrew H. Ko
No relationship to disclose

Anitra Engebretson
Honoraria: AbbVie
Travel, Accommodations, Expenses: AbbVie

Joseph M. Herman
Consulting or Advisory Role: Merrimack Pharmaceuticals, BTG International, OncoSil Medical
Research Funding: Nucletron, BTG International
Patents, Royalties, Other Intellectual Property: CRG

John H. Strickler
Consulting or Advisory Role: Amgen, Marval Biosciences, Onyx Pharmaceuticals, Celgene, Genentech, Bayer, Boehringer Ingelheim
Research Funding: AbbVie (Inst), Gilead Sciences (Inst), MethylGene (Inst), Genentech (Inst), Exelixis (Inst), Bayer (Inst), OncoMed Pharmaceuticals (Inst), Sanofi (Inst), Regeneron Pharmaceuticals (Inst), MedImmune (Inst), Eisai (Inst), Daiichi Sankyo

Al B. Benson III
Consulting or Advisory Role: Genentech, Sanofi, Bristol-Myers Squibb, Merck Serono, Merck/Schering-Plough, Spectrum Pharmaceuticals, Eli Lilly/ImClone Systems, Celgene, Genomic Health, National Cancer Institute, Vicus Therapeutics, Pharmacyclics, Helomics, Taiho Pharmaceutical, Bayer, Alchemia, Infinity Pharmaceuticals, Boehringer Ingelheim, Astellas Pharma, EMD Serono, IntegraGen
Research Funding: Genentech (I), Gilead Sciences, Amgen, Astellas Pharma, Advanced Accelerator Applications, Bayer/Onyx, Novartis, Alchemia, AVEO Pharmaceuticals, Infinity Pharmaceuticals, Merck Serono (Inst), EMD Serono (Inst)
Travel, Accommodations, Expenses: Genentech, Eli Lilly/ImClone Systems, Bayer, Sanofi, Spectrum Pharmaceuticals, AVEO Pharmaceuticals, Gilead Sciences, Astellas Pharma

Susan Urba
Honoraria: Eisai, Merck; Consulting or Advisory Role: Eisai, Merck
Travel, Accommodations, Expenses: Eisai, Merck

Nelson S. Yee
Consulting or Advisory Role: Bayer

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the Journal of Clinical Oncology Web site.

Availability of Companion Documents

The following are available:

- Locally advanced, unresectable pancreatic cancer: American Society of Clinical Oncology clinical practice guideline. Methodology supplement. Alexandria (VA): American Society of Clinical Oncology; 2016. 18 p. Available from the American Society of Clinical Oncology (ASCO) Web site.
- Locally advanced, unresectable pancreatic cancer: American Society of Clinical Oncology clinical practice guideline. Data supplement. Alexandria (VA): American Society of Clinical Oncology; 2016. 45 p. Available from the ASCO Web site.
- Locally advanced, unresectable pancreatic cancer: American Society of Clinical Oncology clinical practice guideline. Slide set. Alexandria (VA): American Society of Clinical Oncology; 2016. 26 p. Available from the ASCO Web site.
- Locally advanced, unresectable pancreatic cancer: American Society of Clinical Oncology clinical practice guideline. Summary of recommendations. Alexandria (VA): American Society of Clinical Oncology; 2016. 4 p. Available from the ASCO Web site.

Patient Resources

The following is available:

- Pancreatic cancer - treatment options. Patient information. 2016 May 31. Available from the Cancer.Net Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on October 27, 2016.

Copyright Statement

Disclaimer

NGC Disclaimer

The National Guideline Clearinghouseâ„¢ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.